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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,851	09/19/2003	Peter Bodine	AHP98134 P1	6790

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EXAMINER	
XIE, XIAOZHEN	
ART UNIT	**PAPER NUMBER**
1646	
MAIL DATE	**DELIVERY MODE**
06/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,851	BODINE, PETER	
	Examiner	Art Unit	
	XIAOZHEN XIE	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6-21 and 26-43* is/are pending in the application.

4a) Of the above claim(s) *7-19 and 26-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Fig.1 of Ruben priority, sequence alignments (3).

DETAILED ACTION

Response to Amendment

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's amendments of the specification filed on 5 February 2009, and the claims filed 6 April 2009 have been entered. Applicant's remarks submitted on 6 April 2009 are acknowledged.

Claims 2, 5 and 22-25 are cancelled. Claims 1, 3, 4, 6-21 and 26-43 are pending. Claims 7-19 and 26-43 are withdrawn from further consideration as being drawn to a nonelected invention. Claims 1, 3, 4, 6, 20 and 21 are under examination.

Specification

The objection to the specification for failing to update the status of related applications is withdrawn in response Applicant's amendment of the specification filed 5 February 2009.

Claim Rejections Withdrawn

The rejection of claims 1-4, 6, 20, 21 and 24 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement, is withdrawn in response to Applicant's amendment of the claims.

The rejection of claim 2 under 35 U.S.C. § 103(a), as being unpatentable over Rubin et al. (US 2003/0175864), in view of Chan et al. (J. Biol. Chem., 1992, 267(35):25202-25207), is withdrawn in response to Applicant's cancellation of the claim.

Claim Rejections Maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 4, 6, 20 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Umansky et al. (U. S. Patent No: 6,433,155 B1, which was filed on 24 September 1997). The basis for the rejection has been set forth in the previous office actions and as the following.

Applicant argues that Umansky does not expressly teach pharmaceutical compositions comprising antibodies capable of specifically binding SEQ ID NO: 2. Applicant argues that while the Office Action identifies fragments of SARP-2 in Umansky that allegedly have overlapping homologous regions with SEQ ID NO: 2, the Office Action, however, fails to establish that those overlapping regions are epitopes for each antigen and that their presentation in the native state of the protein is identical. Applicant argues that while an antibody that binds SARP-2 might perhaps also bind the

polypeptide of SEQ ID NO: 2, this is not necessarily the case. Applicant argues that claim 20 unambiguously recites an antibody that is capable of specifically binding to the polypeptide of SEQ ID NO: 2. The claims do not recite an antibody that binds to a fragment or homologue of SEQ ID NO: 2 and as such, the claimed antibodies do not necessarily bind to the Umansky' s SARP-2.

Applicants' argument has been fully considered but has not been found to be persuasive.

The amended claim 1 recites "*A pharmaceutical composition comprising an antibody generated using SEQ ID NO: 2 as an immunogen, wherein the antibody promotes bone-forming activity in a mammal.*" The amended claim 20 recites "*A pharmaceutical composition for regulating bone-forming activity in a mammal comprising at least one antibody capable of specifically binding SEQ ID NO: 2 and wherein the antibody is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1*".

Umansky et al. teach a pharmaceutically acceptable composition comprising an antibody against a polypeptide of SARP, e.g., SARP-2 (also known as sFRP-1) (col. 3, lines 22-28; col. 4, lines 51-58). The polypeptide of SARP-2 in Umansky et al. shares a 99.7% similarity to the SEQ ID NO: 2 of the instant application; and the two polypeptides differ by one residue over the full-length of 314 amino acids (sequence alignment provided herein, also provided previously). Further, the region spanning amino acid residues 217-231 is identical between the two polypeptides; and this peptide region was used to generate an antibody exhibiting the recited specificity and activities

(see Example 14 of the instant specification). Umansky et al. teach that the antibodies (polyclonal or monoclonal) are generated by using a SARP as an antigen, and by standard methods including the step of immunizing an animal with an antigen containing an antigenic portion of an SARP (col. 15, lines 27-34). Because of the similarity between the two polypeptides (i.e., differing by one residue over the full length of 314 amino acids, and having an identical amino acid sequence between residues 217-231), one of ordinary skill in the art would be so recognized that a substantial population of the antibodies encompassed by the prior art would be identical to the instant antibodies generated using SEQ ID NO: 2 as an immunogen; and that the prior art has at least one antibody capable of specifically binding to SEQ ID NO: 2, and capable of promoting bone-forming activity and inhibiting cell death mediated by overexpression of the polynucleotide of SEQ ID NO: 1. Such is not established by probabilities or possibilities, it is necessarily present in the prior art. The pool of antibodies generated against SARP-2 inherently includes the claimed antibody, because the relevant art provides that "the size of an epitope is approximately equivalent to 5-7 amino acids" (In: Benjamini et al., 1991, Immunology: A Short Course, 2nd ed., see page 40). An alignment between the prior art polypeptide with the instant SEQ ID NO: 2 reveals the identical regions or epitopes, including the region between amino acids 217-231. Therefore, the antibodies generated against SARP-2 inherently include an antibody that specifically binds to SEQ ID NO: 2 and that exhibits the recited activity.

With regard to the limitation of "*an antibody generated using SEQ ID NO: 2 as an immunogen*" in claim 1, case law has long established that a product made by any other

process renders a product-by-process claim unpatentable. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). As set forth above, Umansky et al.'s product anticipates claim 1. With regard to the limitation of "capable of specifically binding SEQ ID NO: 2" in claim 20, the specification does not define for the term "specifically binding"; thus, it does not limit the antibodies only binding to SEQ ID NO: 2. While Umansky et al. do not expressly teach that the antibody promotes bone-forming activity, such as regulating bone growth or bone density, and the antibody is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1, these activities would reasonably be considered to be inherent to the antibody, because the prior art teaches the same antibody and its pharmaceutical uses. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)).

Claims 1, 3, 4, 6, 20 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Rubin et al. (U. S. Patent No: 6,479,255 B1, which was filed on 29 May 1998). The basis for the rejection has been set forth in the previous office actions and as the following.

Applicant argues that while the Office Action identifies fragments of Rubin et al. that have overlapping homologous regions with SEQ ID NO: 2, the Office Action fails to establish that those overlapping regions are epitopes for each antigen and that their presentation in the native state of the protein is identical. Applicant argues that while an antibody that binds to a sequence in Rubin et al. might perhaps also bind the

polypeptide of SEQ ID NO: 2, this is not necessarily the case. Applicant argues that claim 20 unambiguously recites an antibody that is capable of specifically binding to the polypeptide of SEQ ID NO: 2; and the claims do not recite an antibody that binds to a fragment or homologue of SEQ ID NO: 2 and as such, the claimed antibodies do not necessarily bind to the Rubin et al.' s sequences.

Applicants' argument has been fully considered but has not been found to be persuasive.

The amended claims 1 and 20 are as set forth above.

Ruben et al. teach compositions comprising an anti-FRP antibody and a pharmaceutically acceptable carrier, and their pharmaceutical uses (col. 4, lines 39-43; col. 8, lines 18-28; col. 10, lines 6-13; col. 18, lines 21-32). Rubin et al. teach that the anti-FRP antibody specifically recognizes and binds an epitope on a FRP; and that the antibody can be generated using the full-length or an epitope of the FRP polypeptide (col. 14, lines 45-64). Ruben et al. teach the amino acid sequence of the FRP protein, which shows 96.5% similarity to the instant SEQ ID NO: 2, and the region spanning amino acid residues 217-231 is identical between the two polypeptides (this peptide region was used to generate an antibody exhibiting the recited specificity and activities, see Example 14 of the instant specification) (sequence alignment provided herein, also provided previously). In light of the relevant art as discussed above, given the similarity between the two polypeptides, one of ordinary skill in the art would be so recognized that a substantial population of the antibodies encompassed by the prior art would be identical to the instant antibodies generated using SEQ ID NO: 2 as an immunogen; and

the prior art has "at least one antibody capable of specifically binding to SEQ ID NO: 2, and capable of promoting bone-forming activity and inhibiting cell death mediated by overexpression of the polynucleotide of SEQ ID NO: 1". Such is not established by probabilities or possibilities, it is necessarily present in the prior art. Also, for the same reasons as set forth above, Ruben et al.'s product anticipates claim 1 which is directed to a product-by-process; Ruben et al.'s product anticipates claim 20 which recites an antibody capable of "specifically binding" SEQ ID NO: 2; and Ruben et al.'s product inherently possesses the activities as recited in the claims.

Claims 1, 3, 4, 6, 20 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Rubin et al. ("Ruben II") (US 2003/0175864 A1, which has a priority filing date on 29 May 1997), for reasons made of record and reasons set forth herein.

Applicant argues that the sequence referred to as "SEQ ID NO: 3" in Rubin II first appears in its current form in the filing of Rubin II; in other words, SEQ ID NO: 3 in Rubin II is not supported by the application from which it claims priority to. Applicant argues that the earliest date which SEQ ID NO: 3 in Rubin II is entitled to is May 3, 2002 (i.e. Rubin II's filing date); in contrast, the pending claims in the present application are fully entitled to at least the priority date of PCT/US00/25035 (of which the instant application is the national phase filing), which is September 13, 2000.

Applicants' argument has been fully considered but has not been found to be persuasive.

The US 2003/0175864 publication (Ruben II) was filed on 3 May 2002, which claims priority to Application No: 09/087,031, filed on 29 May 1998; and claims priority to provisional Application No: 60/050,417 (filed 29 May 1997) and Application No: 60/050,495 (filed 23 June 1997). The amino acid sequence set forth in SEQ ID NO: 3 is disclosed, at least in Application No: 09/087,031 and in provisional Application No: 60/050,417. In both priority applications, the sequence is disclosed in Figure 1C (Fig. 1 attached herein). The amino acid sequence of Fig. 1C is **identical** to the instant SEQ ID NO: 2 (the Examiner has visually compared the two sequences). Therefore, the SEQ ID NO: 3 his supported in the related applications to which it claims priority to. Accordingly, Ruben II qualifies as prior art.

As set forth previously, Rubin II teaches anti-FRP antibody compositions and their pharmaceutical uses [0058] [0107]. Rubin II teaches that the antibodies can be generated by using the full-length recombinant FRP polypeptide [0090], and the FRP polypeptide of Ruben II is identical to the instant SEQ ID NO: 2 (sequence alignment provided herein, also provided previously). While Ruben II does not expressly teach that the antibody promotes bone-forming activity, such as regulating bone growth or bone density, in a mammal; and the antibody is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO: 1, these activities would reasonably be considered to be inherent to the antibody, because the prior art teaches the same antibody and its pharmaceutical uses. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). Thus, Rubin II anticipates the instant claims.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.
June 16, 2009

/Xiaozhen Xie/